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File 5:Biosis Previews(R) 1969-2003/Sep W4
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Set	Items	Description
S1	2	GLOBIN AND (SUBSTITUTION (2W) CYSTEINE)
S2	39	ALPHA AND (SUBSTITUTION (2W) CYSTEINE)
S3	1	(ALPHA()GLOBIN) AND (SUBSTITUTION (2W) CYSTEINE)
S4	115	E1-E3
S5	7	S4 AND CYSTEINE

? t s1/7/1-2

1/7/1
DIALOG(R)File 5:Biosis Previews(R)
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12966574 BIOSIS NO.: 200100173723
The heme-%%%globin%%% and dimerization equilibria of recombinant human hemoglobins carrying site-specific beta chains mutations.
AUTHOR: Gattoni Maurizio; Piro Maria Cristina; Boffi Alberto; Brinigar William S; Fronticelli Clara; Chiancone Emilia(a)
AUTHOR ADDRESS: (a)CNR Center of Molecular Biology, Department of Biochemical Sciences, University "La Sapienza", Piazza Aldo Moro 5, 00185, Rome: cfrontic@jhmi.edu, emilia.chiancone@uniroma1.it**Italy
JOURNAL: Archives of Biochemistry and Biophysics 386 (2):p172-178 February 15, 2001
MEDIUM: print
ISSN: 0003-9861
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The heme-%%%globin%%% and dimer-tetramer equilibria of ferric recombinant human hemoglobins with site-specific beta chain mutations at the heme pocket or at either the alphalbeta1 or the alphalbeta2 interfaces have been determined. The heme pocket mutation V67T leads to a marked stabilization of the beta chain heme and does not affect the dimer-tetramer association constant, K2,4. In the C112 mutants, the intrinsic rate of beta chain heme loss with respect to recombinant HbA (HbA-wt) is significantly increased only in C112G with some heme released also from the alpha chains. Gel filtration experiments indicate that the K2,4 value is essentially unaltered in C112G and C112L, but is increased in C112V and decreased in C112N. %%%Substitution%%% of %%%cysteine%%% 93 with A or M leads to a slight decrease of the rate of beta chain heme release, whereas the obvserved K2,4 value is similar to that obtained for HbA-wt. Modifications in oxygen affinity were observed in all the mutant hemoglobins with the exception of V67T, C93A, and C112G. The data indicate that there is no correlation between tetramer stability, beta chain heme affinity, and hemoglobin functionality and therefore point to a separate regulation of these properties.

1/7/2
DIALOG(R)File 5:Biosis Previews(R)
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04697535 BIOSIS NO.: 000080000660
A NEW HEMOGLOBIN VARIANT HEMOGLOBIN NUNOBIKI NOTABLE INFLUENCE OF THE CARBOXYL-TERMINAL CYSTEINE ON VARIOUS PHYSICOCHEMICAL CHARACTERISTICS OF HEMOGLOBIN
AUTHOR: SHIMASAKI S
AUTHOR ADDRESS: DEP. BIOCHEM., KAWASAKI MED. SCH., 577 MATSUSHIMA, KURASHIKI, OKAYAMA 701-01, JPN.
JOURNAL: J CLIN INVEST 75 (2). 1985. 695-701. 1985
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A new Hb variant, Hb Nunobiki, was detected in a Japanese male with marginal erythrocytosis. The Hb Nunobiki component amounted to 13.1% of the total Hb. Structural analysis of this variant established the %%%substitution%%% of a %%%cysteine%%% for an arginine at the carboxy terminus of the .alpha.-chain (.alpha.141). The O2 equilibrium curves of Hb Nunobiki revealed extremely high O2 affinity with a reduced Hill coefficient n, a decreased alkaline Bohr effect, and a decreased 2,3-diphosphoglyceric acid effect. The isoelectric point of the Hb Nunobiki changed during storage, although the HbO2 state was maintained. These findings could be accounted for by the specific characteristics of a newly introduced cysteinyl residue. Cysteinyl residue at .alpha.141 in Hb Nunobiki did not seem to be involved in the formation of either intermolecular or intramolecular disulfide bonds under physiologic conditions. The low proportion of Hb Nunobiki (13.1%) in the prospositus was also discussed after it was verified that he exhibited 4 .alpha.-%%%globin%%% genes/diploid cell.

? t s3/7/1

3/7/1
DIALOG(R)File 5:Biosis Previews(R)

04697535 BIOSIS NO.: 000080000660
A NEW HEMOGLOBIN VARIANT HEMOGLOBIN NUNOBIKI NOTABLE INFLUENCE OF THE CARBOXYL-TERMINAL CYSTEINE ON VARIOUS PHYSICOCHEMICAL CHARACTERISTICS OF HEMOGLOBIN
AUTHOR: SHIMASAKI S
AUTHOR ADDRESS: DEP. BIOCHEM., KAWASAKI MED. SCH., 577 MATSUSHIMA, KURASHIKI, OKAYAMA 701-01, JPN.
JOURNAL: J CLIN INVEST 75 (2). 1985. 695-701. 1985
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A new Hb variant, Hb Nunobiki, was detected in a Japanese male with marginal erythrocytosis. The Hb Nunobiki component amounted to 13.1% of the total Hb. Structural analysis of this variant established the %%%substitution%%% of a %%%cysteine%%% for an arginine at the carboxy terminus of the .alpha.-chain (.alpha.141). The O2 equilibrium curves of Hb Nunobiki revealed extremely high O2 affinity with a reduced Hill coefficient n, a decreased alkaline Bohr effect, and a decreased 2,3-diphosphoglyceric acid effect. The isoelectric point of the Hb Nunobiki changed during storage, although the HbO2 state was maintained. These findings could be accounted for by the specific characteristics of a newly introduced cysteinyl residue. Cysteinyl residue at .alpha.141 in Hb Nunobiki did not seem to be involved in the formation of either intermolecular or intramolecular disulfide bonds under physiologic conditions. The low proportion of Hb Nunobiki (13.1%) in the prospositus was also discussed after it was verified that he exhibited 4 .%%%alpha%%% .-%%%globin%%% genes/diploid cell.

? t s5/7/1-7

5/7/1
DIALOG(R)File 5:Biosis Previews(R)

14415637 BIOSIS NO.: 200300409666
A recombinant polymeric Hb as a potential oxygen transporter in therapeutics.
AUTHOR: Bobofchak Kevin M(a); Toshiaki Mito(a); Texel Sarah J(a); Masaaki Nemoto(a); Traystman Richard J(a); Koehler Raymond C(a); Brinigar William S; %%%Fronticelli Clara%%%(a
AUTHOR ADDRESS: (a)Johns Hopkins University, 1721 E Madison, Baltimore, MD, 21205, USA**USA
JOURNAL: Biophysical Journal 84 (2 Part 2):p34a February 2003 2003

MEDIUM: print
CONFERENCE/MEETING: 47th Annual Meeting of the Biophysical Society San Antonio, TX, USA March 01-05, 2003
SPONSOR: Biophysical Society
ISSN: 0006-3495
RECORD TYPE: Citation
LANGUAGE: English

5/7/2
DIALOG(R)File 5:Biosis Previews(R)

13189019 BIOSIS NO.: 200100396168
Molecular engineering of a polymer of tetrameric hemoglobins.
AUTHOR: %%%Fronticelli Clara%%%(a); Arosio Daniele; Bobofchak Kevin M; Vasquez Gregory B
AUTHOR ADDRESS: (a)Department of Anesthesiology, Johns Hopkins University School of Medicine, 600 N. Wolfe St., Baltimore, MD, 21287: cfrontic@jhmi.edu**USA
JOURNAL: Proteins 44 (3):p212-222 August 15, 2001
MEDIUM: print
ISSN: 0887-3585
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We have engineered a recombinant mutant human hemoglobin, Hb Prisca beta(S9C+C93A+C112G), which assembles in a polymeric form. The polymerization is obtained through the formation of intermolecular S-S bonds between %%%cysteine%%% residues introduced at position beta9, on the model of Hb Porto Alegre (beta9SerfwdarwCys) (Bonaventura and Riggs, Science 1967;155:800-802). Cbeta93 and Cbeta112 were replaced in order to prevent formation of spurious S-S bonds during the expression, assembly, and polymerization events. Dynamic light scattering measurements indicate that the final polymerization product is mainly formed by 6 to 8 tetrameric hemoglobin molecules. The sample polydispersity Q=0.07+-0.02, is similar to that of purified human hemoglobin (Q=0.02+-0.02), consistent with a good degree of homogeneity. In the presence of strong reducing agents, the polymer reverts to its tetrameric form. During the depolymerization process, a direct correlation is observed between the hydrodynamic radius and the light scattering of the system, which, in turn, is proportional to the mass of the protein. We interpret this to indicate that the hemoglobin molecules are tightly packed in the polymer with no empty spaces. The tight packing of the hemoglobin molecules suggests that the polymer has a globular shape and, thus, allows estimation of its radius. An illustration of an arrangement of a finite number of tetrameric hemoglobin molecules is presented. The conformational and functional characteristics of this polymer, such as heme pocket conformation, stability to denaturation, autoxidation rate, oxygen affinity, and cooperativity, remain similar to those of tetrameric human hemoglobin.

5/7/3
DIALOG(R)File 5:Biosis Previews(R)

12966574 BIOSIS NO.: 200100173723
The heme-globin and dimerization equilibria of recombinant human hemoglobins carrying site-specific beta chains mutations.
AUTHOR: Gattoni Maurizio; Piro Maria Cristina; Boffi Alberto; Brinigar William S; %%%Fronticelli Clara%%%; Chiancone Emilia(a
AUTHOR ADDRESS: (a)CNR Center of Molecular Biology, Department of Biochemical Sciences, University "La Sapienza", Piazza Aldo Moro 5, 00185, Rome: cfrontic@jhmi.edu, emilia.chiancone@uniroma1.it**Italy
JOURNAL: Archives of Biochemistry and Biophysics 386 (2):p172-178 February 15, 2001
MEDIUM: print
ISSN: 0003-9861

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The heme-globin and dimer-tetramer equilibria of ferric recombinant human hemoglobins with site-specific beta chain mutations at the heme pocket or at either the alpha1beta1 or the alpha1beta2 interfaces have been determined. The heme pocket mutation V67T leads to a marked stabilization of the beta chain heme and does not affect the dimer-tetramer association constant, K2,4. In the C112 mutants, the intrinsic rate of beta chain heme loss with respect to recombinant HbA (HbA-wt) is significantly increased only in C112G with some heme released also from the alpha chains. Gel filtration experiments indicate that the K2,4 value is essentially unaltered in C112G and C112L, but is increased in C112V and decreased in C112N. Substitution of %%%cysteine%%% 93 with A or M leads to a slight decrease of the rate of beta chain heme release, whereas the obvserved K2,4 value is similar to that obtained for HbA-wt. Modifications in oxygen affinity were observed in all the mutant hemoglobins with the exception of V67T, C93A, and C112G. The data indicate that there is no correlation between tetramer stability, beta chain heme affinity, and hemoglobin functionality and therefore point to a separate regulation of these properties.

5/7/4

11838224 BIOSIS NO.: 199900084333
Cysteines beta93 and beta112 as probes of conformational and functional events at the human hemoglobin subunit interfaces.
AUTHOR: Vasquez Gregory B; Karavitis Michael; Ji Xinhua; Pechik Igor; Brinigar William S; Gilliland Gary L; %%%Fronticelli Clara%%%(a
AUTHOR ADDRESS: (a)Dep. Biochem. Mol. Biol., Univ. Maryland Med. Sch., 108 N. Greene St., Baltimore, MD 21201**USA
JOURNAL: Biophysical Journal 76 (1 PART A):p88-97 Jan., 1999
ISSN: 0006-3495
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Three variants of tetrameric.human hemoglobin, with changes at the alpha1beta2/alpha2beta1-interface, at the alpha1beta1/alpha2beta2-alpha1beta2interface, and at both interfaces, have been constructed. At alpha1beta2/alpha2beta1-interface the beta93 %%%cysteine%%% was replaced by alanine (betaC93A), and at the alpha1beta1/alpha2beta2-interface the beta112 %%%cysteine%%% was replaced by glycine (betaC112G). The alpha1beta2 interface variant, betaC93A, and the alpha1beta1/beta2 double mutant, beta(C93A+C112G), were crystallized in the T-state, and the structures determined at 2.0 and 1.8 ANG resolution, respectively. A comparison of the structures with that of natural hemoglobin A shows the absence of detectable changes in the tertiary folding of the protein or in the T-state quaternary assembly. At the beta112 site, the void left by the removal of the %%%cysteine%%% side chain is filled by a water molecule, and the functional characteristics of betaC112G are essentially those of human hemoglobin A. At the beta93 site, water molecules do not replace the %%%cysteine%%% side chain, and the alanine substitution increases the conformational freedom of beta146His, weakening the important interaction of this residue with beta94Asp. As a result, when Cl- is present in the solution, at a concentration 100 mM, the Bohr effect of the two mutants carrying the beta93CysfwdarwAla substitution, betaC93A and beta(C93A+C112G), is significantly modified being practically absent below pH 7.4. Based on the crystallographic data, we attribute these effects to the competition between beta94Asp and Cl- in the salt link with beta146His in T-state hemoglobin. These results point to an interplay between the betaHis146-betaAsp94 salt bridge and the Cl- in solution regulated by the Cys present at position beta93, indicating yet another role of beta93 Cys in the regulation of hemoglobin function.

5/7/5
DIALOG(R)File 5:Biosis Previews(R)

10819619 BIOSIS NO.: 199799440764
Effects of %%%cysteine%%% substitutions in the beta-chains of human Hb.
AUTHOR: Karavitis M(a); Vasquez G(a); Nie W(a); Brinigar W; Gilliland G(a); %%%Fronticelli C%%%(a
AUTHOR ADDRESS: (a)Univ. Md., College Park, MD**USA
JOURNAL: Biophysical Journal 72 (2 PART 2):pA86 1997
CONFERENCE/MEETING: 41st Annual Meeting of the Biophysical Society New Orleans, Louisiana, USA March 2-6, 1997
ISSN: 0006-3495
RECORD TYPE: Citation
LANGUAGE: English

5/7/6
DIALOG(R)File 5:Biosis Previews(R)

09338666 BIOSIS NO.: 199497347036
Effect of %%%cysteine%%% substitution on enthalpy of oxygen binding to recombinant hemoglobins.
AUTHOR: %%%Fronticelli C%%%; Lu A-L; Karavitis M; Shoaee N
AUTHOR ADDRESS: Univ. Maryland Med. Sch., Dep. Biochem., Baltimore, MD 21201**USA
JOURNAL: FASEB Journal 8 (7):pA1294 1994
CONFERENCE/MEETING: 85th Annual Meeting of the American Society for Biochemistry and Molecular Biology Washington, D.C., USA May 21-25, 1994
ISSN: 0892-6638
RECORD TYPE: Citation
LANGUAGE: English

5/7/7
DIALOG(R)File 5:Biosis Previews(R)

03533780 BIOSIS NO.: 000073036860
MOLECULAR DYNAMICS OF HEMO GLOBIN SUBUNITS AS SEEN BY FLUORESCENCE SPECTROSCOPY
AUTHOR: OTON J; BUCCI E; STEINER R F; %%%FRONTICELLI C%%%; FRANCHI D; MONTEMARANO J; MARTINEZ A
AUTHOR ADDRESS: DEP. OF BIOL. CHEM., UNIV. OF MARYLAND MED. SCHOOL, BALTIMORE, MARYLAND 21201.
JOURNAL: J BIOL CHEM 256 (14). 1981. 7248-7256. 1981
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Fluorescent conjugates of [human] .beta.A subunits and their respective heme-free derivatives were prepared in which a 1,5-N-iodoacetylaminoethyl-5-naphthylamine-1-sulfonate probe was specifically placed at the .beta.-93 or .beta.-112 %%%cysteine%%%. The fluorescence anisotropy decay and static fluorescence polarization of these conjugates were examined. Fluorescence measurements were also made using 1-anilino-8-naphthalenesulfonate complexes and the intrinsic fluorescence of the tryptophan groups. For the cases of the .beta.-93 and .beta.-112 conjugates there is substantial evidence for internal rotational freedom of the subunits. The internal mobility of the polypeptide is especially pronounced for the .beta.-112 conjugate. The 1-anilino-8-naphthalenesulfonate probe placed within the heme pocket shows no indication of any rotation other than that associated with the entire .beta.-subunit. Tryptophan fluorescence was measured for the apo-.beta. subunits and for the peptides .beta.(1-55) from Hb A and S. Perrin-Weber plots show the presence of multiple rotational modes suggesting mobility of the tryptophan groups.
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    $97.00  Estimated total session cost   1.696 DialUnits
Logoff: level 03.02.02 D  08:03:29
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